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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/678,997	10/04/2000	Michael David Bentley	34848/194868	4896

826 7590 02/25/2003

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EXAMINER
STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
2637	14

DATE MAILED: 02/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/678,997	Applicant(s) BENTLEY ET AL.	
	Examiner Teresa E Strzelecka	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-56* is/are rejected.

7)☒ Claim(s) *50 and 54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply* .

DETAILED ACTION

1. Receipt is acknowledged of a request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e) and a submission, filed on November 22, 2002. The request has been granted and amendment filed on August 30, 2002 (paper No. 10) has been entered. Applicants arguments were considered.

2. Applicants amended claims 30, 31, 33, 35, 36, 45, 49 and 50, and added new claims 51-56. Claims 30-56 are pending and will be considered in this Office action.

3. Rejections of claims 30, 49 and 50 under 35 U.S.C. 112, second paragraph, are maintained. All other rejections from paper No. 7 are withdrawn in view of the amendment and arguments.

Sequence Rules Compliance

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

APPLICANT IS GIVEN time of reply to this Office action WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.F.R.. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

The following pages contain peptide sequences without SEQ ID NOs: page 6, lines 30, 31; page 7, lines 13, 15; page 15, line 18; page 16, line 3; page 17, lines 7 and 28.

Claim Objections

5. Claims 50 and 54 objected to because of the following informalities:

A) Claim 50 recites "... polymer is absent lipophilic moieties...". At the very least this is a very awkward phrase which could be substituted with "polymer lacks lipophilic moieties".

B) Claim 54 recites "... polymer is absent fatty acids and glycolipids...". At the very least this is a very awkward phrase which could be substituted with "polymer lacks fatty acids and glycolipids".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 30-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 30, 49 and 50 are indefinite over the recitation of a limitation "...substantially hydrophilic conjugate...". It is not clear what degree of hydrophilicity is considered "substantial", especially since the only guidance provided by the specification is that "...By the term "substantially hydrophilic" it is intended to mean that the conjugate of this invention does not contain a substantially lipophilic moiety..." (page 5, lines 20-25), without definition of what "substantially lipophilic" means.

B) Claim 31 is indefinite over the recitation of "...the native peptide...". There is no term "native peptide" in claim 30, from which claim 31 depends. Also, two peptides are claimed in claim 30, biphalin and [D-Pen2, D-Pen5] enkephalin, so it is not clear which would be the native one.

C) Claim 36 is indefinite over the recitation of "... said peptide is covalently linked at one of its N-termini to said polymer..." (emphasis added). Peptides or proteins usually contain one N-terminus and one C-terminus, so it is not clear what it means for a peptide to have more than one N-terminus.

D) Claim 51 is indefinite over the recitation of "... covalently linked to a water soluble, nonpeptidic polymer is selected from...". This seems to be a typographical error, where another word is missing between "polymer" and "is".

Response to Arguments

8. Applicant's arguments filed August 30, 2002 have been fully considered but they are not persuasive. Applicants argue that the rejection of claims 30, 49 and 50 under 35 U.S.C. 112, second paragraph, should be withdrawn because one would understand that "substantially hydrophilic" means not containing a substantially lipophilic moiety, and that Applicants defined substantially lipophilic moieties as fatty acids or glycolipids.

This argument is not found persuasive for the following reasons. "The term "lipophilic" means the ability to dissolve in lipids, and the term "hydrophilic" means the ability to dissolve in water. Therefore, what does it mean for a polymer to be "substantially hydrophilic"? For example, to what degree does the polymer have to be water-soluble to be considered substantially hydrophilic? Applicants did not provide guidance for determining that degree. The degree of hydrophilicity would also depend on the ratio of hydrophilic to lipophilic groups. For example, a

single cholesterol molecule attached to a high molecular weight PEG molecule might not influence its water solubility, but a long-chain fatty acid might. Applicants provide examples of fatty acids and glycolipids as being substantially lipophilic, whereas other lipophilic molecules include alkyl chains, cholesterol or adamantane. Example of possible confusion as to the meaning of the term "substantially hydrophilic" comes from considering a compound containing both hydrophilic and lipophilic moieties, where the lipophilic moiety is cleaved off once the compound enters the bloodstream (as taught in Ekwuribe et al., U.S. Patent No. 6,309,633). Would this compound be considered as "substantially hydrophilic"?

It is clear that the meets and bounds of the term "substantially hydrophilic" cannot be determined based on Applicants disclosure, therefore the rejection is maintained.

9. No references were found teaching or suggesting claims 30-56, but they are rejected for reasons given above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

February 21, 2003

Teresa Strzelecka, Ph. D.

Patent Examiner

Notice to Comply	Application No.	Applicant(s)	
	09/678,997	BENTLEY ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

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